REMARKS

Claims 29-43 are rejected. Claims 1-28 and 44-64 are withdrawn from consideration. Claims 1-64 are presently pending in the application. Favorable reconsideration of the application in view of the following remarks is respectfully requested.

Rejection Of Claims 29-43 Under 35 U.S.C. §103(a):

The Examiner has rejected Claims 29-43 under 35 U.S.C. 103(a) as being unpatentable over EP 0430371, indicating that the reference discloses a composition comprising monodisperse beads stabilized by vinylsulfonyl functionalized polymers, wherein said vinylsulfonyl functionalized polymers are grafted to the external surfaces of said beads, the polymers employed to form the small beads conform to the general structure -(A)o-(B)p-(D)q, wherein -A- represents units derived from one or more hydrophobic ethylenically unsaturated monomers, -B- represents units derived from vinylsulfonyl group, -D- represents units derived from one or more ethylenically unsaturated monomers which are different than those represented by -A- or -B- with the molar ratios overlapping with the claimed molar ratio in that q can be 0, the polymers have been disclosed as well as specific monodispersed beads, the reference further discloses biological receptors of interest having the requisite free amino or sulfhydryl group for covalent bonding to the small polymer beads, corresponding to the claimed bioaffinity tag (claim 43). The Examiner further indicates that, although the disclosure of the reference differs from the instant claims in that it does not disclose the claimed coefficient of variation in the particle diameter nor the claimed formula I and II, the reference does disclose the requirements of the claims including specific components which are included in the claimed formula to form the product, a particle composition comprising monodisperse polymer beads and, therefore, it would have been obvious to one of ordinary skill in the art to select reactants from the reference within the limitation of the instant claims to form the vinylsulfonyl functionalized polymers of the claimed formulas and products, monodisperse polymer particle comprising a coefficient of variation in the particle diameter, as in the claims, since they have been shown to be effective in a similar system and thus would have been expected to provide adequate results and there is no showing of unexpected results derived from said selection.

EP 0430371 discloses an analytical element for immunoassays comprising a support and a spreading layer characterized in that the element contains a first population of relatively large polymeric beads a second population of relatively small polymeric beads having receptors covalently bound to the bead surface through surface reactive groups and surfaces which are free of residual materials.

The present invention relates to a polymer particle comprising a polymer bead stabilized by vinylsulfonyl-functionalized polymers grafted to the surface of the bead, which are useful in a biological assay to allow a biological capture agent to be easily attached to the surface of such microspheres without using any chemical coupling agents and which allow the tag to retain higher reactivity than the same compounds bound directly to the surface of a similar bead.

To establish a prima facia case of obviousness requires, first, there must be some suggestion or motivation, either in the references themselves, or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references (or references when combines) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in the applicant's disclosure. *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998).

The reference fails to teach the modification required by the present invention, that is, the particles of the present invention contain vinylsulfonyl units, which are part of the particle stabilizer polymer attached to the surface of the bead, but which are not part of the bead itself. The Examiner states "wherein said vinylsulfonyl functionalized polymers are grafted to the external surfaces of said beads (see page 4, lines 5-22). This passages reads:

> *"As already stated, the small polymeric beads have receptors on their surface. The receptors are bonded to the beads through surface reactive groups, which are directly or indirectly reactive with free amino groups, sulfhydryl groups, carboxy groups, aldehyde or ketone groups of the receptors. Useful surface reactive groups include: a) active halogen*

groups; b) activated 2-substituted ethylsulfonyl or activated vinylsulfonyl groups;"

The passage indicates that the vinylsulfonyl groups are surface reactive groups and are part of the polymers of the bead itself, not part of polymers attached to the surface of the bead as presently claimed. In addition, pg. 6, lines 35-43 of the reference read:

"The small polymer beads can be homogeneous particles being composed of the same polymer throughout, or they can be particles composed of more than one polymer such as graft copolymers as described, for example, in U.S. Patent 3,700, 609 and core-shell polymers described for example, in U.S. Patent 4,401, 765. This is advantageous when any of the recurring units of the polymer that must be on the particle surface such as those containing the reactive groups or groups that impart dispersion stability are expensive. A polymer particle can be prepared from relatively inexpensive monomers, or monomers that regulate buoyancy, then polymerization is continued to add a shell of a different polymer having the requisite surface groups."

This passage further indicates that the reactive functionality is part of the particle, not part of a polymer grafted to the surface of the bead. The Examiner also states "the reference further discloses biological receptors of interest having the requisite free amino or sulfhydryl group for covalent bonding to the small polymer beads." As presently claimed, the biological receptors bond to the grafted polymer, not the polymer bead itself.

The reference also fails to provide any likelihood of success, as there is no teaching to suggest that the reactive groups could be incorporated in a polymer attached to the surface of the bead, instead of being part of the bead. The Abstract of the reference also indicates that the bead has "surfaces which are free of residual materials". The present invention has grafted polymers on the surface of the bead, making the present inventive particle a particle with surfaces bearing residual materials.

The reference also fails to include all the limitations of the present invention, as there is no mention of a "vinylsulfonyl-functionalized polymers grafted to the surface of said bead". The reference instead indicates that the polymers bearing the functional groups which "*conform to the general structure -*

(A)o-(B)p-(D)q" are "*employed to form the small beads*" (pg. 4, lines 23-24), instead of polymers grafted to the bead surface.

The present invention also provides surprising results, as the grafted polymers provide a 3-dimensional network of functionality, increasing the number of functional groups which may be associated with the bead, thereby increasing its ability to bind biological targets, as indicated on page 3, lines 17-25 of the present specification:

> *"Macromolecular Rapid Communications Vol. 15 p. 909-915 (1994) reports the immobilization of enzymes to soluble stabilizer polymer arms protruding from the surface of a polymer particle. Enhancements in accessibility of the enzyme to target substrates are observed over enzymes covalently bound directly to the particle surface."*

The particles of the present invention contain vinylsulfonyl units, which are part of the particle stabilizer polymer grafted to the surface of the bead, and hence, allow for attachment of biological macromolecules in a less deactivating manner. Biological macromolecules immobilized on these particles via the soluble stabilizer polymer grafts will retain higher reactivity than the same compounds bound directly to the surface of a similar bead. The present inventive bead also is made via a simpler process than the processes reported in the prior art in which the

> *"the stabilizer arms contained only carboxylic acids as their reactive functionality, so if covalent attachment was desired, it would require the use of a coupling agent and a subsequent preparative step."* (page 3, lines 17-25)

In the present invention,

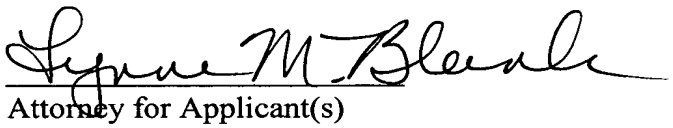
> *". no coupling reagents are needed for the attachment of biological molecules, which greatly simplifies the process of attaching a biological molecule to the microspheres. These polymer particles may show promise for use in biological microarrays due to the very high density of vinylsulfonyl moieties on their surface, their high monodispersity, and the ability to produce larger sized beads."* (pg. 4, lines 25-30)

In summary, the reference fails to disclose, teach or suggest the present invention wherein a vinylsulfonyl-functionalized polymer is grafted to the surface of the bead, fails to provide any likelihood of success for the use of

residual materials present on the bead surface, and fails to include the limitation that vinylsulfonyl-functionalized polymers be grafted to the surface of the bead. In addition, the present invention offers improved biological capture activity as a result of the enhancements in accessibility of the biological target to the functional group, the increased activity as a result of more functional groups presenting association with the bead, and a simpler process of manufacture. The Applicants therefore request that the Examiner reconsider and withdraw the rejection.

It is believed that the foregoing is a complete response to the Office Action and that the claims are in condition for allowance. Favorable reconsideration and early passage to issue is therefore earnestly solicited.

Respectfully submitted,



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